EXHIBIT D

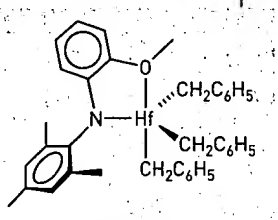
Ron Dagani, "Finding Catalysts Faster: Symyx-Dow collaboration yields new class of polyolefin catalysts", *Chemical and Engineering News*, p.10, April 7, 2003

COMBINATORIAL MATERIALS

FINDING CATALYSTS FASTER

Symyx-Dow collaboration yields new class of polyolefin catalysts

A FOUR-YEAR COLLABORATION between Symyx Technologies and Dow Chemical has borne fruit in the discovery of a new class of single-site catalysts for olefin polymerization. The new amide-ether-based hafnium catalysts were found using a fully integrated high-throughput screening methodology [*J. Am. Chem. Soc.*, 125, 4306 (2003)].



Complex 1

"The results are stunning," says one of the coauthors, Dow chemist James C. Stevens, because the new screening methodology enabled them to do in days or weeks what used to take many months or years.

The Dow-Symyx researchers set out to discover new catalysts with potential for the production of linear low-density polyethylene, which is a copolymer of ethylene and an α-olefin, such as 1-octene. They first synthesized a library of hafnium and zirconium complexes containing 23 different bidentate and tridentate ligands. To screen these complexes under different activation conditions, they carried out 384 polymerization experiments in just a few hours.

The work uncovered many catalytically active metal-ligand combinations. One hafnium catalyst (complex 1) was found capable, under the right conditions, of polymerizing 1-octene with 100% conversion. Further experiments demonstrated that this complex can produce high-molecular-weight ethylene-1-octene copolymers.

In the course of one day, the researchers then studied the activity at 130 °C of 96 other hafnium complexes containing related amine-ether ligands. They found that many of these catalysts are even better at copolymerizing ethylene and 1-octene than complex 1.

In larger scale batch reactor experiments, complex 1 and a closely related hafnium complex were found to perform as well as or better than Dow's workhorse metallocene polyolefin catalyst system.

Dow isn't necessarily "marching to commercialization" with any of the catalysts reported in the *JACS* paper, Stevens tells C&EN. "But we will be talking soon, I think, about another catalyst that's come out of this procedure that is going to be commercialized."—RON DAGANI

PRION INSIGHTS

BOUND TO WORK

Form of normal prion protein binds to and inhibits infectious form in vivo

FOR THE FIRST TIME IN LIVE animals, researchers have shown that a form of normal prion protein binds to abnormal prion protein—the cause of Creutzfeldt-Jakob disease, mad cow disease, and other prion diseases. Their experiments also indicate how infectious prions might be inhibited.

It has been proposed that prion disease spreads when infectious prion protein (PrP^{Sc}, prion protein scrapie) exerts a bad influence on normal prion protein (PrP^{C}, prion protein cellular), making it too turn bad. To have such an influence, the infectious prion presumably has to first bind with PrP^{C}. This interaction has been demonstrated in vitro, but because of technical obstacles, researchers have not previously been able to show that it occurs in living animals.

Adriano Aguzzi, professor of neuropathology at the University of Zurich, and coworkers now find that when a dimeric form of PrP^{C} is expressed in mice and the animals are given infectious prions, PrP^{C} dimer binds PrP^{Sc} in vivo and slows the onset of prion disease in the mice [*Cell*, 113, 49 (2003)]. The dimer apparently ties up PrP^{Sc}'s binding site, slowing the rate at which it can bind to natural PrP^{C} in the brain and convert it into additional infectious prions.

The study thus helps confirm the protein-only hypothesis of prion disease and points the way toward potential therapeutics. A number of agents that fight prion disease have been found previously, but none of these "worked when prions were applied directly to the brain" as the prion dimer does, Aguzzi says.

The challenge will be to find drugs capable of reaching the brain, where PrP^{Sc} does its damage. "We are trying hard to get there," Aguzzi says. "Preliminary results, not included in the *Cell* paper, are very encouraging."—STU BORMAN

DOUBLE VISION
PrP^{C} dimer expressed in mice by Aguzzi and coworkers.